

SICKLE CELL TRAIT
Information for Physicians and Nurses
Southwestern Comprehensive Sickle Cell Center
October 31, 2007

Sickle Cell Terminology

Sickle cell disease (SCD) is the name for a group of related blood disorders caused by sickle hemoglobin (Hgb S). Upon deoxygenation, Hgb S forms rigid polymers that damage the red blood cell membrane, causing anemia and vaso-occlusion. The most common and severe form of SCD is sickle cell anemia (Hgb SS), the homozygous state for Hgb S. Less frequent forms of SCD result from compound heterozygous states with Hgb S and other hemoglobinopathies, such as Hgb C (sickle-hemoglobin C disease) and β -thalassemia (sickle- β -thalassemia). **Sickle cell trait is the heterozygous or carrier state for Hgb S.**

Frequency of Sickle Trait and SCD

About 2 million people in the United States have **sickle cell trait**. The trait is common among individuals of African ancestry, but it also occurs in individuals of Mediterranean, Middle Eastern, Asian Indian, and Hispanic heritage. Sickle trait occurs rarely in individuals of Northern European descent. Approximately 1:12 African Americans has sickle trait compared to 1:413 Caucasians.

In the US, **sickle cell disease (SCD)** occurs 1:500 African Americans. SCD occurs in many other races and ethnicities, too. SCD occurs in 1:58,000 Caucasians, 1:1,100 Hispanics (eastern states), 1:32,000 Hispanics (western states), 1:11,500 Asians, and 1:2,700 Native Americans.

Newborn Screening for SCD

Screening for hemoglobinopathies in Texas by the Department of State Health Services is done by isoelectric focusing (a type of hemoglobin electrophoresis). Abnormal results that indicate the presence of disease are confirmed by molecular genetic (DNA-based) testing. The most common newborn hemoglobin patterns are shown below (remember that hemoglobins are always reported in order of decreasing predominance).

<u>Pattern</u>	<u>Compatible States</u>
FA	Normal (or thalassemia trait)
FAS	Sickle cell trait
FSA	Sickle- β^+ -thalassemia
FS	Sickle cell anemia or sickle- β^0 -thalassemia
FSC	Sickle-hemoglobin C disease

Newborn screening for sickle cell *disease* also identifies many babies with sickle cell *trait*. Currently, in Texas, only the likely presence of disease, *and not sickle trait*, is reported to the parents. Physicians are notified of all results (trait and disease). The newborn screening program has future plans to report trait status to parents. Until then, healthcare personnel should inform families of the presence of sickle trait in a newborn.

Testing for Sickle Trait in Children and Adults

Unlike newborn screening, a “sickle prep” does not distinguish between the trait and disease. Therefore, sickle trait and SCD must be differentiated by hemoglobin electrophoresis. Hemoglobin electrophoresis is a common test performed by most commercial laboratories.

Significance of Sickle Trait

Individuals with sickle trait are almost always healthy (see below for rare exceptions). **They do not have a disease.** Sickle trait does not cause anemia, microcytosis, splenomegaly, or pain. Further, people with sickle trait *can* donate blood.

It is important, however, for individuals to know that they have the trait, because of the risk to their offspring. Sickle cell anemia (Hgb SS) is an autosomal recessive disease, so if both parents have sickle trait then each of their offspring will have a one-quarter or 25% chance of having sickle cell anemia. Genetic counseling should be offered, and pre-implantation and pre-natal diagnosis is also available.

Genetic Counseling

Counseling is straightforward. Sickle cell disease is a classical autosomal recessive disease. That is, two abnormal genes are needed to produce the disease. Having only one abnormal gene is the asymptomatic trait state. Each parent donates one of two beta-globin (hemoglobin) genes to each offspring. See the examples below.

	A	S
A	AA	AS
A	AA	AS

Example 1: If one parent has S trait (AS) and the other is normal (AA), then offspring have a 50% chance of having trait and a 50% chance of having normal hemoglobin.

	A	S
A	AA	AS
S	AS	SS

Example 2: If both parents have S trait (AS), then offspring have a 25% chance of having normal hemoglobin, a 50% chance of having trait, and a 25% chance of having have sickle cell anemia (SS).

	A	S
A	AA	AS
C	AC	SC

Example 3: If one parent has S trait (AS) and the other has C trait (AC), then offspring have a 25% of having normal hemoglobin, a 50% chance of having trait (either C or S trait), and a 25% chance of having sickle-hemoglobin C disease (SC).*

	A	S
A	AA	AS
T	AT	ST

Example 4: If one parent has S trait (AS) and the other has beta thalassemia trait (AT), then offspring have a 25% of having normal hemoglobin, a 50% chance of having trait (either beta thalassemia trait or S trait), and a 25% chance of having sickle-beta thalassemia (ST).*

**Separate brochures on Hgb C trait and beta thalassemia trait are available upon request.*

Uncommon and Rare Adverse Effects of Sickle Trait

Sickle cell trait on very rare occasions is associated with increased morbidity and mortality. The following rare associations have been reported:

- Splenic infarction at high altitude, with exercise, or with hypoxemia
- Isothenuria with loss of maximal renal concentrating ability
- Hematuria and renal papillary necrosis
- Fatal exertional heat illness with exercise (rhabdomyolysis)
- Sudden idiopathic death with exercise (cardiac arrest)
- Glaucoma or recurrent hyphema following a first episode of hyphema
- Bacteruria in women
- Bacteruria or pyelonephritis associated with pregnancy
- Renal medullary carcinoma in adolescents and young adults
- Early onset of end stage renal disease from autosomal dominant polycystic kidney disease

The deaths associated with sickle trait occurred under extreme conditions of exertion, heat, and dehydration. Exercise and sports are safe for individuals with sickle trait as long as over-exertion, over-heating, and dehydration are avoided. These should be avoided in children without sickle trait, too.

Contact Information

The Pediatric Sickle Cell Program:
214-456-6102

The hematologist-oncologist on-call:
214-456-2382 (08:00 – 17:00)
214-456-7000 (after hours)